

REMARKS

Introductory Comments:

Claims 21-30 were examined in the Office Action dated June 16, 2006.

Claims 21-30 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Claims 21-22, 24, and 28 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,470,705 to Grossman et al. (Grossman).

Claims 21-25, and 27-29 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 6,027,890 to Ness et al. (Ness) in view of Grossman.

Claim 26 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Grossman.

Claim 30 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Grossman further in view of U.S. Patent No 6,331,530 to Breslow et al. (Breslow).

Claims 21-30 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over U.S. Application No. 10/779,255.

Claims 21-30 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over U.S. Patent No. 6,770,439.

Claims 21-30 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over U.S. Patent No. 7,001,725.

Claims 21-30 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting over U.S. Patent No. 6,673,550.

SUPPORT FOR AMENDMENTS

The applicants have amended the first paragraph of the specification to recite related application information.

Claim 26 has been amended to recite that from 5 to 100 different electrophoretic probes form distinct peaks. The amendment corrects for antecedent basis.

Claim 30 has been amended to not depend from itself. The amendment thus corrects for a minor error.

Accordingly, no new matter has been added by way of this amendment and the entry thereof is respectfully requested.

Addressing the Examiner's Rejections

Rejections of the Claims Under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 21-30 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

The applicants traverse the rejection of the claims because the phrase “aggregation” is said to be vague. The specification, at paragraph 209, for example, provides a definition of the phrase “aggregation” where the proteins may be combined with organelles, cells, viruses, etc. Thus, in view of the knowledge in the field and the disclosure, one of ordinary skill in the art would know what is encompassed by the phrase.

Rejections of the Claims Under 35 U.S.C. §102(b)

The Examiner rejected claims 21-22, 24, and 28 under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 5,470,705 to Grossman et al. (Grossman).

The applicants traverse the rejection. In order for a reference to anticipate an invention, the reference must teach each and every element of the claimed invention. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379, 231 USPQ 81, 90 (Fed. Cir. 1986). *Atlas Powder Co. v. E. I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 411 (Fed. Cir. 1984). Moreover, the single source must disclose all of the claimed elements “arranged as in the claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 9 USPQ 2d 1913, 1920 (Fed. Cir. 1989); *Connell v. Sears Roebuck & Co.*, 722 F.2d 1542, 1548, 220 USPQ 193, 198 (Fed. Cir. 1983). The cited reference does not disclose all the elements of the applicants’ claims.

Claims 21-22, 24, and 28 pertain to electrophoretic probes defined by the formula:



that have a cleavable linkage L and, upon cleavage of L, an eTag reporter comprising a detection group D and a mobility modifier M is produced. Thus, the applicants are claiming electrophoretic probes that upon cleavage at L produce an eTag of formula (D,M).

The Examiner cites Grossman at column 2, lines 54-64, column 6, lines 46-54, and column 20, lines 49-51 as disclosing an anticipatory probe where the probe includes a binding polymer, a polymer chain that imparts to that probe a distinctive ratio of charge/translational frictional drag, and a reporter attached to the binding polymer.

The use of this probe is described at column 20, line 61 to column 21, line 15, and illustrated in Figures 20A-20C. The probes described by Grossman at column 20, lines 49-51

are hybridized to the target polynucleotide under hybridization conditions (column 20, lines 61-67), the non-bound probes are removed by washing (column 21, lines 7-9), and the bound probes then released by denaturation and identified by electrophoresis (column 21, lines 10-15). The Grossman probe **starts and ends** as a probe having “binding polymer **250**, a polymer chain **252** that imparts to that probe a distinctive ratio of charge/translational frictional drag, and a reporter **254** attached to the binding polymer.” The probes disclosed by Grossman at column 20, lines 49-51 are thus not cleaved, and it therefore does not produce an eTag of formula (D,M). Thus, Grossman does not disclose all the limitations of the claims. Therefore, it does not anticipate the claims.

The Examiner states that Grossman at column 20, lines 15-25 discloses a probe that is cleaved by 5' to 3' exonuclease. This is an alternative embodiment of Grossman's invention described in Section D, column 19, line 22 to column 20, line 44 and its use is illustrated in Figures 17A and 17B. The probe includes two target binding regions **190** and **194** that are joined by a single-stranded RNA region **196**, a polymer chain **198** attached to **190**, and a reporter **F** attached to **194**. The probe is hybridized to a target, treated with RNase H which recognizes and cleaves the RNA/DNA duplex, and denatured. This Grossman probe thus starts as **198—190—196—194—F** and produces **198—190—196'** and **196''—194—F**, where **196'** and **196''** represent single-stranded RNA of different lengths. In this alternative embodiment, the cleavage of the Grossman probe produces two fragments with one of the fragments having the mobility modifying polymer chain **198** and the other fragment having the reporter **F**, it does not produce **198—F**. In contrast, applicants are claiming electrophoretic probes defined by the formula $[(D, M)-L]_k-T$ that upon cleavage at **L** produce an eTag of formula (D,M) where **D** is a

detection group, and M is a mobility modifier. Grossman thus does not disclose all the limitations of the claims. Therefore, it does not anticipate the claims.

The cited reference does not disclose all the elements of the claims, and therefore, does not anticipate the applicants' invention. Therefore, the Examiner is respectfully requested to withdraw the rejection.

Rejections of the Claims Under 35 U.S.C. §103(a)

(a) The Examiner rejected claims 21-25, and 27-29 under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 6,027,890 to Ness et al. (Ness) in view of Grossman.

In order for the Office to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references. Second, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. The teachings or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). The cited references do not disclose all the elements of the applicants' claims, therefore, a *prima facie* case of obviousness has not been made.

Ness discloses mass spectrometry tags (column 16, line 27 onwards), infrared tags (column 18, line 41 and onwards), UV tags (column 19, lines 10-29), fluorescent tags (column 19, lines 30-57), and potentiometric tags (column 19, line 58-column 29, line 17). The reference does not disclose eTag reporters of different electrophoretic probes that form distinct peaks upon electrophoretic separation. The Examiner acknowledges that Van Ness does not disclose the

ligand pair having a mobility modifier which produces a unique electrophoretic mobility. As discussed above, Grossman does not disclose electrophoretic probes that upon cleavage of L produce an eTag reporter comprising a detection group, D, and a mobility modifier, M. Grossmann either discloses a set of probes that are not cleaved (column 20, line 61 to column 21, line 15, and Figures 20A-20C), or probes that upon cleavage produce two fragments where one of them has the detection group and the other has the mobility modifier (Section D, column 19, line 22 to column 20, line 44 and Figures 17A and 17B).

Grossman does not disclose a set of electrophoretic probes that overcomes the deficiencies of Van Ness. Thus, the combination of Van Ness and Grossman does not disclose all the elements of the claims 21-25, and 27-29. Accordingly, a *prima facie* case of obviousness has not been presented by the Office. Therefore, the Examiner is respectfully requested to withdraw the rejection.

(b) Claim 26 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Grossman.

The applicants traverse the rejection. Claim 26 ultimately depends from claim 20, and, therefore, contains all the elements of claim 20. Thus, claim 26 claims an electrophoretic probe having a cleavable linkage L. As discussed above, Grossman does not disclose electrophoretic probes that upon cleavage of L produce an eTag reporter comprising a detection group, D, and a mobility modifier, M. Grossmann either discloses a set of probes that are not cleaved (column 20, line 61 to column 21, line 15, and Figures 20A-20C), or probes that upon cleavage produce two fragments where one of them has the detection group and the other has the mobility modifier (Section D, column 19, line 22 to column 20, line 44 and Figures 17A and 17B). The cited reference does not disclose all the elements of the claims, and therefore, a *prima facie* case of

obviousness has not been presented by the Office. Therefore, the Examiner is respectfully requested to withdraw the rejection.

(c) Claim 30 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Grossman further in view of U.S. Patent No 6,331,530 to Breslow et al. (Breslow).

The applicants traverse the rejection. Breslow is cited to show that singlet oxygen is produced to cleave the linker. In Breslow, two β -cyclodextrin molecules joined by a cleavable linker are cleaved upon exposure to light, and the released molecules are not electrophoretically separated but instead used to kill tumor cells. Breslow does not disclose electrophoretic probes having a cleavable linkage L. As discussed above, Grossman also does not disclose electrophoretic probes having a cleavable linkage L. Thus, the combination of Grossman and Breslow would not provide all the elements of claim 30. Accordingly, a *prima facie* case of obviousness has not been presented by the Office. Therefore, the Examiner is respectfully requested to withdraw the rejection.

Provisional Rejections of the Claims Under Double Patenting

Claims 21-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Application No. 10/779,255. The applicants will consider filing a terminal disclaimer upon indication of allowable subject matter.

Claims 21-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Patent No. 6,770,439. The applicants will consider filing a terminal disclaimer upon indication of allowable subject matter.

Claims 21-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Patent No. 7,001,725. The applicants will consider filing a terminal disclaimer upon indication of allowable subject matter.

Claims 21-30 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of U.S. Patent No. 6,673,550. The applicants will consider filing a terminal disclaimer upon indication of allowable subject matter.

CONCLUSION

Applicants respectfully submit that the claims define an invention that is patentable over the art, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicants' representative at (650) 335-7818.

Respectfully submitted,
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